IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	Group Art Unit: 1645
SCHASTEEN *et al.*	)	
	)	
Application No.: 10/799,083	)	Examiner: Vanessa L. Ford
	)	
Filed: March 12, 2004	)	
	)	Confirmation No. 8520
For: METHODS AND COMPOSITIONS FOR THE CONTROL OF COCCIDIOSIS	)	

Attention: Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPEAL BRIEF

In support of the Notice of Appeal filed January 25, 2010, and 37 C.F.R. § 41.37, the Appellant presents this Appeal Brief and hereby authorizes the Commissioner to charge any and all extensions or fees that may be required to Deposit Account No. 50-1662. Submitted herewith is also a request for a three (3) month extension of time, extending the period of time for submitting the Appeal Brief from March 25, 2010, to June 25, 2010. The Appeal Brief responds to the Final Action mailed October 28, 2009, which resulted in final rejection of claims 2-6, 8-13, 23-26, and 102.

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I. REAL PARTY IN INTEREST

Novus International, Inc., is the real party in interest.

II. RELATED APPEALS AND INTERFERENCES

The Appellant is unaware of any pending appeals or interferences that may directly affect or be directly affected by, or have a bearing on, the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

Claims 2-6, 8-13, 23-26, and 102 are pending in this application. Claims 1-7, 14-16, 19-22, and 27-101 were previously withdrawn without prejudice. Claims 17-18 were previously cancelled without prejudice.

Claims 2-6, 8-13, 23-26, and 102 have been finally rejected by the Examiner. The Appellant hereby appeals the rejection of claims 2-6, 8-13, 23-26, and 102. In accordance with 37 C.F.R. 41.37 (c)(1)(viii), a clean copy of the claims on appeal are set forth in full in the Claims Appendix to this brief.

IV. STATUS OF AMENDMENTS

No amendments to the claims have been filed after the final rejection.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to methods for separating and/or isolating viable oocysts by the use of a hydrocyclone.[1, 2, 3] The present invention also provides methods for the sporulation, sterilization, separation, and storage of coccidial oocysts, without the use of potassium dichromate.[4, 5] The invention further comprises a method for preparing a vaccine for the prevention and/or control of coccidiosis comprising viable sporulated oocysts.[6] Written description support for independent claims 3, 5, and 6 is provided below.

Claim 3: A method of separating viable oocysts[7] from a liquid suspension[8] by the use of a hydrocyclone.[9, 10, 11]

Claim 5: A method for isolating oocysts comprising:

collecting manure from host animals wherein said manure contains viable[12] oocysts known to cause coccidiosis[13];

diluting said manure in an aqueous medium to create a slurry;[14]

separating unwanted fecal matter from said slurry and collecting the aqueous fraction containing viable[15] oocysts;[16]

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[1] See, *e.g.*, originally filed specification at page 28, paragraph [0084].
[2] See, *e.g.*, originally filed specification at page 26, paragraph [0078].
[3] See, *e.g.*, originally filed claim 3 at page 72 of the specification.
[4] See, *e.g.*, originally filed specification at page 7, paragraph [0018].
[5] See, *e.g.*, originally filed claims 3, 5, an 6 at pages 72-73 of the specification.
[6] See, *e.g.*, originally filed specification at pages 7-8, paragraph [0021].
[7] See, e.g. originally filed specification at paragraphs [0021]-[0028]. See also paragraphs [0039], [0040], and [0045].
[8] See, *e.g.*, originally filed claim 3 at page 72 of the specification.
[9] See, *e.g.*, originally filed specification at page 28, paragraph [0084].
[10] See, *e.g.*, originally filed specification at page 26, paragraph [0078].
[11] See, *e.g.*, originally filed claim 3 at page 72 of the specification.
[12] See, e.g. originally filed specification at paragraphs [0021]-[0028]. See also paragraphs [0039], [0040], and [0045].
[13] See, *e.g.*, *Id.*
[14] See, *e.g.*, originally filed claim 5 at page 72 of the specification.
[15] See, e.g. originally filed specification at paragraphs [0021]-[0028]. See also paragraphs [0039], [0040], and [0045].
[16] See, *e.g.*, originally filed claim 5 at page 72 of the specification.

subjecting said aqueous fraction to separation by means of a hydrocyclone.[17]

Claim 6: A method for isolating viable[18] oocysts comprising:

collecting manure from host animals wherein said manure contains viable[19] oocysts known to cause coccidiosis[20];

diluting said manure in an aqueous medium to create a slurry; [21]

separating unwanted fecal matter from said slurry and collecting the aqueous fraction containing viable[22] oocysts; [23]

subjecting said aqueous fraction to separation by means selected from the group consisting of a centrifuge and a hydrocyclone, and collecting the solid phase; [24]

combining a dense aqueous liquid with said collected solid phase wherein said dense liquid has a density greater than about 1.09 g/ml and wherein the viable[25] oocysts are buoyant; [26]

subjecting the combination of said dense aqueous liquid and collected solid phase to centrifugation and collecting the dense liquid fraction containing viable[27] oocysts; [28]

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[17] See, *e.g.*, *Id.*
[18] See, e.g. originally filed specification at paragraphs [0021]-[0028]. See also paragraphs [0039], [0040], and [0045].
[19] See, *e.g.*, *Id.*
[20] See, *e.g.*, *Id.*
[21] See, *e.g.*, originally filed claim 6 at pages 72-73 of the specification.
[22] See, e.g. originally filed specification at paragraphs [0021]-[0028]. See also paragraphs [0039], [0040], and [0045].
[23] See, *e.g.*, originally filed claim 6 at pages 72-73 of the specification.
[24] See, *e.g.*, *Id.*
[25] See, e.g. originally filed specification at paragraphs [0021]-[0028]. See also paragraphs [0039], [0040], and [0045].
[26] See, *e.g.*, originally filed claim 6 at pages 72-73 of the specification.
[27] See, e.g. originally filed specification at paragraphs [0021]-[0028]. See also paragraphs [0039], [0040], and [0045].
[28] See, *e.g.*, originally filed claim 6 at pages 72-73 of the specification.

diluting said dense liquid fraction to a specific gravity wherein the viable[29] oocysts are no longer buoyant; [30]

separating viable oocyst solids from said liquid fraction by means of a hydrocyclone and re-collecting the solid phase. [31]

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Claims 2-6, 8-10, and 23-26 stand rejected under 35 U.S.C. § 103(a) over Conkle *et al.* (WO 00/50072) and Alesina *et al.* (SU 1637882; Abstract Translation).

B. Claims 11-13 stand rejected under 35 U.S.C. § 103(a) over Conkle *et al.* and Alesina *et al.*, and further in view of Sjoerdsma *et al.* (U.S. Patent No. 4,399,151).

C. Claim 102 stands rejected under 35 U.S.C. § 103(a) over Conkle *et al.*, Alesina *et al.*, Sjoerdsma *et al.*, and further in view of Kimura *et al.* (*Journal of Protozoology Research*, July 2000).

VII. ARGUMENT

The Examiner maintains the rejections of 2-6, 8-13, 23-26, and 102. The arguments set forth below will address each basis of rejection under separate subheadings, in accordance with 37 C.F.R. 41.37(c)(1)(vii).

The Appellant will demonstrate herein that a *prima facie* case of obviousness has not been established or, alternatively, that any *prima facie* case of obviousness has been rebutted. Among other considerations, it will be shown that the prior art has been cited out of context. When the prior art is considered in its entirety, it is apparent that there would have been no motivation to combine or reasonable expectation of success in combining the references in the manner cited by the Office. Importantly, the cited references include several portions

[29] See, e.g. originally filed specification at paragraphs [0021]-[0028]. See also paragraphs [0039], [0040], and [0045].
[30] See, *e.g.*, originally filed claim 6 at pages 72-73 of the specification.
[31] See, *e.g.*, *Id.*

that, taken as a whole, lead away from the claimed invention and contradict a finding of obviousness. It will also be shown that the methods of the claimed invention yield unexpected results, which support a finding of nonobviousness.

For the purposes of this Appeal, claims 2-6, 8-13, 23-26, and 102 are under appeal and are submitted to stand or fall together. The Appellant respectfully asserts that the Office has failed to establish a *prima facie case* of obviousness, particularly with regard to the use of a "hydrocyclone" for separaing/isolating "viable oocysts" as presently claimed.

A. The Evidence of Record Supports the Nonobviousness of the Currently Claimed Invention

One of the key issues relating to the patentability of the currently claimed invention is whether, at the time of filing, it would have been predictable or foreseeable to use a hydrocyclone for the purposes of the currently claimed invention. Thus far, the Office has found no reference or rationale that reasonably teaches or suggests the use of a hydrocyclone for separating/isolating viable oocysts. The Office has only cited to references that disclose other types of methods of isolating oocysts (*e.g.*, Conkle) or discuss using a hydrocyclone to isolate other kinds of materials (*e.g.*, Alesina abstract).

Importantly, the grounds for rejection asserted by the Office are not based on a rational underpinning and would not have provided a reasonable expectation of success at the time of filing. The evidence of record indicates that the currently claimed invention was surprising and unpredictable over the prior art. In particular, the prior art taught away from such a combination since a hydrocyclone was previously expected to fatally damage the oocysts due to the intense sheer forces.

> "[0084] In yet another embodiment, a hydrocyclone is used to concentrate the filtrate obtained from sieving. It has been discovered that a hydrocyclone, traditionally used in the petrochemical and environmental science fields is useful for

> concentrating oocysts. Hydrocyclones use the principle of centrifugal separation to remove or classify solid particles from a fluid, based on size, shape, and density. The use of a hydrocyclone, not known to be used for living organisms, was previously believed to fatally damage the oocysts due to intense sheer forces. The instant invention provides a method of utilizing a hydrocyclone to concentrate oocysts." Paragraph [0084], Originally Filed Patent Specification. (Emphasis Added).

As noted in the Applicant's Office Action Response filed December 29, 2008, this teaching away is further highlighted by the Conkle reference relied upon by the Office.

> "Overall, the agitation level should be sufficient to fully suspend all solids during sporulation but not enough to destroy the oocysts. This may occur through aeration, shaking, stirring, and combinations thereof." Conkle *et al*. page 7, lines 31-33. (Emphasis Added).

As such, the Examiner's response in view of Svennson *et al.* that "oocysts . . . are considered to be very resistant to physical and chemical agents"[32] is submitted to be error and inconsistent with the Conkle reference relied upon in all of the pending § 103 rejections.

Importantly, the Svensson reference refers to encysted oocysts in a different coccidial life stage and in a different context, and the Examiner's application of Svensson is respectfully asserted to be mistaken. As provided by the Applicant's own specification, the life cycle of the coccidial parasite is complex.[33] Whereas the oocysts in a different life stage may be resistant, the currently claimed "viable oocysts" used for vaccines are known in the art to be extremely fragile and condition-sensitive. In view of the above, it is respectfully submitted that the prior art does not disclose, teach, or suggest the currently

[32] See, *i.e.*, Final Action at page 5, lines 12-15.
[33] See, *e.g.*, originally filed specification at page 1, paragraph [0003]. (Emphasis Added).

claimed invention, which recites methods for separating a viable oocyst using a hydrocyclone.

In addition, the previously submitted evidence of record, including the declaration of Dr. Christopher Knight and Dr. Julia Dibner attached hereto, establish with specificity why the currently claimed invention was unexpected and surprising over the prior art. As experts in the field of the currently claimed invention, neither Dr. Knight nor Dr. Dibner believed that a hydrocyclone could be used for the purposes of the currently claimed invention, since it was known that viable oocysts were sensitive to physical and chemical stresses. (See, *e.g.*, an excerpt provided below of the Dr. Knight and Dr. Dibner Declaration filed August 3, 2009).

> 4. Through our employment at Novus as indicated above, we both are familiar with and have supervised portions of the research and development efforts that resulted in the discovery of the methods currently claimed in the '391 application. At the outset of the project, we were skeptical that hydrocyclones could be used to isolate viable oocysts. To be useful for the production of a live-vaccine, the oocysts are required to be viable following isolation. Oocysts, however, were known in the art to be extremely fragile and destroyed by agitation, stirring, or even by the mechanical action of digestion. See, *e.g.*, newly identified supporting references showing the general state of the art, including U.S. Patent No. 4,808,404 ("The sporozoites of *Eimeria* species once out of their protective shells, *i.e.*, oocysts and sporocysts, are very fragile and lose their infectivity within a few days."); U.S. Patent No. 6,891,024 ("Oocysts and sporocysts are found in the intestinal contents but the fragile oocyst is commonly disrupted by the time feces are passed."); and U.S. Patent No. 6,998,126 ("The wall of the sporulated oocyst is ruptured by the mechanical action in the gizzard and intestinal tract . . ."). Our experience at Novus International in handling oocysts further confirms that they are extremely fragile and subject to rupture.

Notably, "viable oocysts" are also described in the Applicant's patent specification as being sensitive/susceptible to physical and chemical stresses ("The sporulated oocysts are viable for up to about 18 hours." See, *e.g.*, originally filed specification at page 17, paragraph [0052]. "Lower temperatures, about 4 degrees C, are preferred when sieving procedures take over more than three hours to protect the viability of the oocysts." See, *e.g.*, originally filed specification at page 25, at paragraph [0077]. "Sporulated oocysts which had not

been sterilized, however, showed a rapid decrease in viability when stored." See, *e.g.*, originally filed specification at page 86, paragraph [0184].").

Accordingly, these fragile viable oocysts would not be recognized by a skilled artisan as being as "very resistant to physical and chemical agents," as maintained by the Office in the Final Action. These fragile "viable oocysts," as described by Conkle and observed by Dr. Knight and Dr. Dibner, bear no relation to the "very resistant" oocysts asserted by the Office. Considering that Dr. Knight and Dr. Dibner are experts in the field, and that the Conkle reference validates the fragile nature of the viable oocysts, the Applicant respectfully asserts that the Office is mistaken on this key issue of fact and respectfully requests reversal of the current rejections.

Moreover, the previously submitted declaration of Dr. Knight and Dr. Dibner further explains that, even in view of Alesina, a skilled artisan would not have had a reasonable expectation of success in applying a hydrocyclone to viable oocysts. The reasons include the substantial differences in size, density, and overall morphology between "viable oocysts" and microorganisms such as bacteria, explained below.

> 6. In the recent Office Action concerning the '391 application, mailed on June 24, 2009, the Patent Office cites to a new reference referred to as Alesina *et al.* (SU 19984621763; "Alesina"). The abstract provided of Alesina refers to a hydrocyclone for use in microorganism suspension separation. The reference, however, makes no mention whether the microorganism suspension would be live or dead before or after separation. Furthermore, the term "microorganism" is not an art-recognized equivalent of oocysts, since oocysts are more akin to fertilized eggs, which are not yet developed enough to be infective. Physically, oocysts are also much larger and less dense than microorganisms such as bacteria, including structural differences in the outer membrane/cell wall that make oocysts substantially more fragile than bacteria. Consequently, oocysts would not be considered to be the same or substantially similar to the term "microorganisms" as set forth by the Patent Office.

The Office has provided no rebuttal evidence regarding the differences between the "viable oocysts" of the currently claimed invention versus generic microorganisms such as bacteria.

The evidence of record also shows that the cited Alesina reference

discusses microorganisms without any discussion of the unique problems or associated obstacles of isolating fragile oocysts. Moreover, the abstract translation of Alesina provided by the Office provides no information whether the generic microorganisms would be live or dead following use of the hydrocyclone. Although the Examiner concludes that one of skill in the art "would not reasonably conclude . . . that the microorganism used in their invention are dead"[34] – this assertion lacks any factual support. The Alesina is completely silent as to whether the microorganisms would be dead or alive, ruptured or whole, and provides no instructions as to how to modify the process for extremely fragile oocysts. On the contrary, Alesina is not a reliable indication of the state of the art when it is contradicted by Dr. Knight, Dr. Dibner, and the Conkle reference, all of which are more germane to vaccines for coccidiosis and the currently claimed invention.

Thus far, the Office has failed to acknowledge that the "viable oocysts" of the currently claimed invention, as noted in the declaration above, the written specification, and the Conkle reference, are extremely fragile. The Office has thus far ignored the Applicant's rebuttal evidence and declaration, including that a skilled artisan's knowledge of the oocyst fragility would: (1) teach away from using a hydrocyclone as currently claimed; (2) provide no motivation to combine for the reasons as asserted by the Office; and, (3) would have provided no reasonable expectation of success in using a hydrocyclone to isolate viable oocysts at the time of filing. In short, the Applicant respectfully submits that the Office's assertion that the viable oocysts of the currently claimed invention are "very resistant to physical and chemical agents" is flatly refuted by the evidence of record.

With regard to the claims currently pending before the Board, the Applicant respectfully asserts that the facts speak for themselves, and that the currently claimed invention is unexpected/surprising over the prior art. Reversal

[34] See, *i.e.*, Final Action mailed October 28, 2009, at page 6, lines 1-3.

of the rejections is respectfully requested.

B. The Rejection of Claims 2-6, 8-10, and 23-26 under 35 U.S.C. § 103(a) over Conkle *et al.* (WO 00/50072) and Alesina *et al.* (SU 1637882; Abstract Translation) Is Improper

Claims 2-6, 8-10, and 23-26 stand rejected under 35. U.S.C. § 103(a) over Conkle and Alesina. At page 3, lines 10-30, the Final Action states, "Conkle et al. teach methods of isolating and separating oocysts from Eimeria species (oocysts known to cause coccidiosis) (See the Abstract). . . . Conkle et al. teach that a need exists for a more efficient vaccination method. . . . Conkle et al. do not teach the use of hydrocyclones." (Emphasis Added). At page 4, lines 1-8, the Final Action states, "Alesina et al. teach hydrocyclones can be used for microorganism suspension separation (see the Abstract)." Alesina does not specifically teach using a hydrocyclone to separate viable oocysts.

To reject a claim under § 103, the cited art combination must teach or suggest all claim limitations, there must be a reason to combine the cited references based on a rational underpinning, and there also must be a reasonable expectation of success to arrive at the claimed invention. Herein, the Appellant will show that each of these statutory requirements of § 103 has not been met. Notably, there is no reason based on a rational underpinning to combine the Conkle and Alesina references. In fact, Conkle teaches away from combination with the Alesina references. Further, even if the Conkle and Alesina references were combined, there would be no reasonable expectation of success to arrive at the Appellant's currently claimed invention.

As provided above, the Appellant's specification, evidence of record, and submitted declaration support that the "viable oocysts" of the currently claimed invention are extremely fragile. This fact is further supported by the Conkle reference at page 7, lines 31-33, which state that oocysts may be destroyed through aeration, shaking, stirring, and combinations thereof. The Examiner has not provided any persuasive rebuttal evidence as to this particular point. The

Svennson reference does not refer to "viable oocysts" being isolated for the purposes of a vaccine. Rather Svennson refers to a different coccidial life stage, in which the oocysts are encysted in a protective coating. As such, taken in context, the Svennson reference is not indicative of the "viable oocysts" of the currently claimed invention. Whereas Svensson "is only used to establish the state of the art",[35] it only establishes the state of the art regarding a different coccidial life stage and is therefore immaterial to the currently claimed invention. By contrast, the evidence of record, including the declaration of Dr. Knight and Dr. Dibner, as well as the teachings of the Conkle reference, indicate that a hydrocyclone would not have been a predictable solution with regard to fragile "viable oocysts."

The Examiner's argument to "apply a known technique to a known product to be used in a known method" is factually mistaken. It is not obvious to use a method with intense sheer forces to a product that is extremely fragile. When the fragility of the product is further confirmed by one of the cited § 103 references (here: Conkle), there is: (1) no motivation to combine the references; (2) an express teaching away; and (3) no reasonable expectation of success.

MPEP 2143.02 requires a reasonable expectation of success to arrive at the currently claimed invention. In light of the Supreme Court's instruction in *KSR*, the Federal Circuit has stated that, "[t]o the extent an art is unpredictable, as the chemical arts often are, *KSR*'s focus on 'identified, predictable solutions' may present a difficult hurdle because potential solutions are less likely to be genuinely predictable." *Eisai Co. Ltd. v. Dr. Reddy's Labs.*, Ltd, 533 F.3d 1353, 1359 (Fed. Cir. 2008). (Emphasis Added). Importantly, an obviousness determination requires that a skilled artisan would have perceived a reasonable expectation of success in making the invention in light of the prior art. In the present circumstance, the Examiner has failed to make an adequate finding of fact regarding whether it would have been reasonable to combine a hydrocyclone

[35] See, *e.g.*, Final Action at page 6, lines 10-12.

(extreme sheer forces) with viable oocysts that are extremely fragile.

As provided by the MPEP, references cannot be combined where a reference teaches away from their combination. MPEP 2145(D)(2) states, "It is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983) (The claimed catalyst which contained both iron and an alkali metal was not suggested by the combination of a reference which taught the interchangeability of antimony and alkali metal with the same beneficial result, combined with a reference expressly excluding antimony from, and adding iron to, a catalyst.)." In the present case, because the oocysts of Conkle are recited to be destroyed through aeration, shaking, stirring, and combinations thereof, the Conkle reference teaches away from using the hydrocyclone of Alesina.

Furthermore, the Appellant respectfully asserts that MPEP 2143.01(II) requires the Examiner to consider when one cited reference discredits or undercuts the basis for rejection. MPEP 2143.01(II) states, "The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and all teachings in the prior art must be considered to the extent that they are in analogous arts. Where the teachings of two or more prior art references conflict, the examiner must weigh the power of each reference to suggest solutions to one of ordinary skill in the art, considering the degree to which one reference might accurately discredit another. *In re Young*, 927 F.2d 588, 18 USPQ2d 1089 (Fed. Cir. 1991)." Here, the Applicant respectfully asserts that the Board consider the entirety of the prosecution record, including the Conkle reference which provides teachings away, undercuts the Examiner's assertion that viable oocysts are "very resistant," and refutes any reasonable expectation of success for applying hydrocyclones to viable oocysts.

The Office's citation of the *KSR* precedent in the Final Action at page 4, lines 9-25, is similarly misapplied. Importantly, *KSR* states, "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support

the legal conclusion of obviousness.'" *KSR*, 550 U.S. at 398, 82 USPQ2d at 1396 quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)." In the present case, there is no rational underpinning to the asserted rejection. At the time of filing, a skilled artisan would have no motivation or expectation of success in applying the "hydrocyclone" of Alesina to viable oocysts because hydrocyclones use extreme sheer forces. Nothing in Alesina provides any teachings or suggestions that it may be used to separate live microorganisms or whether the microorganisms remain intact following separation. Moreover, even microorganisms such as bacteria would be considered to be more resistant than the extremely fragile oocysts of the currently claimed invention, and as such, Alesina is not substantially germane or relevant to the currently claimed invention.

The Appellant respectfully asserts that the rejection of claims 2-6, 8-10, and 23-26 under 35. U.S.C. § 103(a) over Conkle and Alesina has been overcome. Reversal is respectfully requested.

C. The Rejection of Claims 11-13 under 35 U.S.C. § 103(a) over Conkle *et al.* (WO 00/50072) and Alesina *et al.* (SU 1637882; Abstract Translation) and further in view of Sjoerdsma et al. (U.S. Patent No. 4,399,151) Is Improper

Claims 11-13 stand rejected under 35. U.S.C. § 103(a) over Conkle and Alesina as applied to claims 2-6, 8-10, and 23-26, and further in view of Sjoerdsma et al. At page 6, lines 18-24, the Final Action states, "Conkle et al. have been described previously. Conkle et al. and [Alesina] do not teach the use of screens. Sjoerdsma et al teach that mesh screens can be used to extract debris from biological material (Example 6, column 24)." Again, the Office cites to *KSR* for the proposition that, "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."

The arguments above are hereby incorporated and reasserted with

respect to claims 11-13 and the currently pending rejections. Claims 11-13 are dependent upon claim 6 and if there was no reasonable expectation of success and no motivation to combine with regard to the base claim, there is also no reasonable expectation of success with regard to dependent claims 11-13. Reliance on Sjoerdsma, however, is misplaced as the cited reference does not refer to the separation of any viable oocysts or any living organism, but only a mixture of 2-difluoromethyl-2,5-diaminopentanoic acid, corn starch, lactose, and zinc stearate. Importantly, Sjoerdsma et al. does not disclose, teach, or suggest use of a hydrocyclone to separate viable oocysts. The reference only discloses that mesh screens can be used to extract debris from a starch paste (See Sjoerdsma et al., Example 6, column 24, lines 28-34).

The Examiner's argument to "apply a known technique to a known product to be used in a known method" is mistaken. It is not obvious to use a method with intense sheer forces to a product that is extremely fragile. The fragile nature of the viable oocysts is confirmed by the evidence of record, as well as the Conkle reference. In view of all of the above, there is: (1) no motivation to combine the references; (2) an express teaching away; and (3) no reasonable expectation of success.

The Appellant respectfully asserts that the rejection of claims 11-13 under 35. U.S.C. § 103(a) over Conkle, Alesina, and Sjoerdsma has been overcome. Reversal is respectfully requested.

D. The Rejection of Claim 102 under 35 U.S.C. § 103(a) over Conkle *et al.* (WO 00/50072), Alesina *et al.* (SU 1637882; Abstract Translation) and Sjoerdsma *et al.* (U.S. Patent No. 4,399,151), and further in view of Kimura *et al.* (Journal of Protozoology Research, July 2000) Is Improper

Claim 102 stands rejected under 35. U.S.C. § 103(a) over Conkle, Alesina, and Sjoerdsma as applied above. At page 8 of the Final Action, the Office acknowledges that "Conkle et al. and Alesina et al. do not teach the claim

limitation 'the method of claim 6 wherein the dense aqueous liquid is selected from the group consisting of sucrose and fructose corn syrup.'" The Final Action further asserts "Kimura et al. teach a flotation technique using sucrose (see the Abstract). Kimura et al teach that the sucrose flotation technique is a fast on-step simple and inexpensive method that allows from the separation and recovery of oocysts (see the Abstract)."

The arguments above are hereby incorporated and reasserted with respect to claim 102 and the currently pending rejections. Claim 102 is dependent upon claim 6 and if there was no reasonable expectation of success and no motivation to combine with regard to the base claim, there is also no reasonable expectation of success with regard to dependent claim 102. The defect in the Office's obviousness rejection is not cured by resort to Kimura et al., either alone or in combination with Conkle or Alesina. The Office Action states that "Kimura et al teach a flotation technique using sucrose (see the Abstract). . ." However, as with the other cited art, Kimura fails to disclose, teach, or suggest any use of a hydrocyclone to separate viable oocyst, as currently claimed. Even in the flotation technique of Kimura, "the recovery rate from high turbidity water was significantly lower," which is considered a teaching away from the currently claimed invention. At the time of filing, there would have been no expectation of success in using a hydrocyclone to separate a viable oocyst, since such a method would have been expected to fatally damage the oocysts. As such, Kimura et al., either alone or in combination with Conkle et al. and Alesina et al. fail to disclose, teach, or suggest all elements that are recited in claim 102.

The Examiner's argument to "apply a known technique to a known product to be used in a known method" is mistaken. It is not obvious to use a method with intense sheer forces to a product that is extremely fragile. The fragile nature of the viable oocysts is confirmed by the evidence of record, as well as the Conkle reference. In view of all of the above, there is: (1) no motivation to combine the references; (2) an express teaching away; and (3) no reasonable expectation of success.

The Appellant respectfully asserts that the rejection of claim 102 under 35. U.S.C. § 103(a) over Conkle, Alesina, Sjoerdsma, and Kimura has been overcome. Reversal is respectfully requested.

E. Conclusion

For the foregoing reasons, the Appellant respectfully submits that the currently pending claims are patentable and in condition for allowance. Accordingly, the Appellant respectfully requests that the current grounds of rejection be reversed. The Commissioner is hereby authorized to change any and all fees that may be required or credit any overpayment to Deposit Account No. 50-1662.

Polsinelli Shughart PC

Respectfully submitted,

Date: June 25, 2010

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Attorney for Appellant

Claims Appendix to Appeal Brief Under Rule 47.37(c)(1)(viii)

Claim 1 (withdrawn): A method for producing a composition for the prevention or control of coccidiosis comprising:

collecting manure from host animals wherein said manure contains oocysts known to cause coccidiosis;

diluting said manure in an aqueous medium to create a slurry;

separating unwanted fecal matter from said slurry and collecting the aqueous fraction containing oocysts;

subjecting said aqueous fraction to solid/liquid phase centrifugal-based separation and collecting the solid phase;

combining a dense aqueous liquid with said collected solid phase wherein said dense liquid has a density greater than about 1.09 g/ml and wherein the oocysts are buoyant;

subjecting the combination of said dense aqueous liquid and collected solid phase to centrifugation and collecting the dense liquid fraction containing oocysts;

diluting said dense liquid fraction to a specific gravity wherein the oocysts are no longer buoyant;

separating oocyst solids from said diluted liquid fraction by centrifugal-based separation and re-collecting the solid phase.

Claim 2 (previously presented): A method as set forth in claim 6 further comprising:

diluting said re-collected solid phase in an aqueous sporulation medium;

sporulating said viable oocysts while in contact with said sporulation medium;

separating sporulated oocysts from said sporulation medium;

sterilizing said sporulated oocysts; and

diluting said sporulated oocysts to form a vaccine composition.

Claim 3 (previously presented): A method of separating viable oocysts from a liquid suspension by the use of a hydrocyclone.

Claim 4 (previously presented): A method as set forth in claim 3 wherein the viable oocysts are collected in the underflow from the hydrocyclone.

Claim 5 (previously presented): A method for isolating oocysts comprising:

collecting manure from host animals wherein said manure contains viable oocysts known to cause coccidiosis;

diluting said manure in an aqueous medium to create a slurry;

separating unwanted fecal matter from said slurry and collecting the aqueous fraction containing viable oocysts;

subjecting said aqueous fraction to separation by means of a hydrocyclone.

Claim 6 (previously presented): A method for isolating viable oocysts comprising:

collecting manure from host animals wherein said manure contains viable oocysts known to cause coccidiosis;

diluting said manure in an aqueous medium to create a slurry;

separating unwanted fecal matter from said slurry and collecting the aqueous fraction containing viable oocysts;

subjecting said aqueous fraction to separation by means selected from the group consisting of a centrifuge and a hydrocyclone, and collecting the solid phase;

combining a dense aqueous liquid with said collected solid phase wherein said dense liquid has a density greater than about 1.09 g/ml and wherein the viable oocysts are buoyant;

subjecting the combination of said dense aqueous liquid and collected solid phase to centrifugation and collecting the dense liquid fraction containing viable oocysts;

diluting said dense liquid fraction to a specific gravity wherein the viable oocysts are no longer buoyant;

separating viable oocyst solids from said liquid fraction by means of a hydrocyclone and re-collecting the solid phase.

Claim 7 (withdrawn): A method for isolating oocysts comprising:

collecting feces from animals wherein said feces contains oocysts known to cause coccidiosis;

contacting said feces with an aqueous medium;

separating unwanted fecal matter from said oocysts;

subjecting said oocysts to centrifugal-based separation and collecting the oocyst-containing solid fraction;

suspending the oocyst-containing solid fraction in a flotation solution;

allowing the oocysts to separate from the solids, wherein the oocysts are floated to the top of the solution; and

removing the flotation medium from said oocysts by tangential flow filtration.

Claim 8 (previously presented): A method as set forth in claim 6 wherein said animals comprise the class Aves.

Claim 9 (previously presented): A method as set forth in claim 8 wherein said slurry is created by mixing about 0.5 gallons to about 5 gallons of domestic water per the amount of manure obtained in about 3 days from about six animals comprising the class Aves.

Claim 10 (original): A method as set forth in claim 9 wherein said animals are chickens.

Claim 11 (previously presented): A method as set forth in claim 6 wherein said separation of unwanted fecal matter comprises sieving.

Claim 12 (original): A method as set forth in claim 11 wherein said sieving is by use of multiple-tier shaker screens.

Claim 13 (original): A method as set forth in claim 12 wherein said shaker screens comprise a 50-mesh screen and a 250-mesh screen.

Claim 14 (withdrawn): A method as set forth in claim 1 wherein said method is carried out at a temperature between about 4° C and about 30° C.

Claim 15 (withdrawn): A method as set forth in claim 14 wherein said sieving is carried out at a temperature between about 22° C and about 28° C.

Claim 16 (withdrawn): A method as set forth in claim 15 wherein said sieving is carried out at about 25° C.

Claim 17 - 18 (cancelled).

Claim 19 (withdrawn): A method as set forth in claim 18 wherein said centrifugal-based separation comprises the use of a centrifuge.

Claim 20 (withdrawn): A method as set forth in claim 19 wherein said centrifuge is a bottle centrifuge.

Claim 21 (withdrawn): A method as set forth in claim 19 wherein said centrifuge is a continuous centrifuge.

Claim 22. (withdrawn): A method as set forth in claim 6 wherein said centrifugation is a bottle centrifuge.

Claim 23 (previously presented): A method as set forth in claim 6 wherein said dense aqueous liquid comprises a solution of corn syrup or sodium chloride.

Claim 24 (previously presented): A method as set forth in claim 6 wherein said dense aqueous liquid has a density from about 1.09 g/ml to about 1.20 g/ml.

Claim 25 (previously presented): A method as set forth in claim 24 wherein said dense aqueous liquid has a density from about 1.09 g/ml to about 1.14 g/ml.

Claim 26 (previously presented): A method as set forth in claim 25 wherein said dense aqueous liquid has a density from about 1.09 g/ml to about 1.10 g/ml.

Claim 27 (withdrawn): A method for inducing sporulation of oocysts comprising:

introducing into an aqueous sporulation medium oocysts of at least one species of protozoa known to cause coccidiosis;

incubating said oocysts in said aqueous sporulation medium, thereby causing sporulation of oocysts; and

introducing an oxidizing agent into said medium at a rate sufficient to maintain the average dissolved oxygen content during sporulation at least 30% of saturation.

Claim 28 (withdrawn): A method as set forth in claim 27 wherein said dissolved oxygen content is substantially maintained at between about 30% and about 80% of saturation throughout the period of sporulation.

Claim 29 (withdrawn): A method as set forth in claim 28 wherein said dissolved oxygen content of the medium is substantially maintained at between about 40% and about 60% of saturation throughout the period of sporulation.

Claim 30 (withdrawn): A method as set forth in claim 29 wherein said dissolved oxygen content of the medium is substantially maintained at about 50% of saturation.

Claim 31(withdrawn): A method as set forth in claim 27 wherein the alkali metal dichromate content of said sporulation medium is less than about 0.8% by weight during incubation of oocysts.

Claim 32 (withdrawn): A method as set forth in claim 27 comprising addition to said sporulation medium of an oxidizing agent having a standard reduction potential of at least about 0.5 V.

Claim 33 (withdrawn): A method as set forth in claim 32 comprising addition of both molecular oxygen and another oxidizing agent.

Claim 34 (withdrawn): A method as set forth in claim 33 wherein said oxidizing agent has a standard reduction potential of at least about 0.5 V.

Claim 35 (withdrawn): A method as set forth in claim 34 wherein said oxidizing agent is selected from the group consisting of an alkali metal hypochlorite, an alkali metal chlorite, an alkali metal chlorate, an alkali metal perchlorate, and an alkali metal permanganate.

Claim 36 (withdrawn): A method as set forth in claim 35 wherein said oxidizing agent comprises hypochlorite ions.

Claim 37 (withdrawn): A method as set forth in claim 35 wherein a sufficient amount of an alkali metal hypochlorite is added to achieve an alkali metal hypochlorite weight percent from about 0.001 weight percent to about 0.1 weight percent of the sporulation medium and oocysts combined, wherein said alkali metal hypochlorite is from about 1.0 % to about 10.0 % by volume.

Claim 38 (withdrawn): A method as set forth in claim 27 further comprising:

separating sporulated oocysts from said sporulation medium;

sterilizing sporulated oocysts by contacting said sporulated oocysts with a chemical disinfectant; and

storing said sporulated oocysts in a sterile diluent, said diluent containing less than about 0.8% by weight alkali metal dichromate.

Claim 39 (withdrawn): A method as set forth in claim 27 wherein said medium contains less than about 0.3% by weight dichromate ion during incubation of said oocysts.

Claim 40 (withdrawn): A method as set forth in claim 27 wherein said medium contains less than about 0.15% by weight hexavalent chromium during incubation of said oocysts.

Claim 41 (withdrawn): A method as set forth in claim 27 wherein said dissolved oxygen content is established by bubbling an oxygen-containing gas through said sporulation medium.

Claim 42 (withdrawn): A method as set forth in claim 41 wherein said oxygen-containing gas consists essentially of air.

Claim 43 (withdrawn): A method as set forth in claim 41 wherein said gas comprises commercially pure oxygen.

Claim 44 (withdrawn): A method as set forth in claim 27 further comprising maintaining the temperature from a temperature that substantially avoids freezing to about 45° C.

Claim 45 (withdrawn): A method as set forth in claim 44 wherein temperature is maintained from about 15° C to about 40° C.

Claim 46 (withdrawn): A method as set forth in claim 45 wherein temperature is maintained from about 20° C to about 30° C.

Claim 47 (withdrawn): A method as set forth in claim 46 wherein temperature is maintained at about 28° C.

Claim 48 (withdrawn): A method as set forth in claim 27 further comprising incubating the oocysts under said conditions from about 72 hours to about 120 hours.

Claim 49 (withdrawn): A method as set forth in claim 48 wherein the oocysts incubate from about 72 hours to about 96 hours.

Claim 50 (withdrawn): A method as set forth in claim 49 wherein the oocysts incubate for about 72 hours.

Claim 51 (withdrawn): A method as set forth in claim 27 further comprising controlling the pH of the sporulation medium.

Claim 52 (withdrawn): A method as set forth in claim 51 wherein the pH is controlled by the introduction of an acid or base to the sporulation medium.

Claim 53 (withdrawn): A method as set forth in claim 52 wherein the pH of the sporulation medium is controlled by alternatively adding sodium hydroxide and sulfuric acid to the sporulation medium.

Claim 54 (withdrawn): A method as set forth in claim 53 wherein the pH of the sporulation medium is controlled from about 7.2 to about 7.5.

Claim 55 (withdrawn): A method as set forth in claim 54 wherein the pH of the sporulation medium is controlled at about from 7.35 to about 7.45.

Claim 56 (withdrawn): A method as set forth in claim 38 wherein said sporulated oocysts are separated from said sporulation medium by filtration or by centrifugal-based separation.

Claim 57 (withdrawn): A method as set forth in claim 56 wherein said sporulated oocysts are separated by filtration.

Claim 58 (withdrawn): A method as set forth in claim 57 wherein said sporulated oocysts are separated from the sporulation medium by tangential flow filtration.

Claim 59 (withdrawn): A method as set forth in claim 38 wherein said sterilization is achieved by adding a chemical disinfectant to sporulated oocysts separated from said sporulation medium.

Claim 60 (withdrawn): A method as set forth in claim 59 wherein said sterilization substantially eliminates microorganisms.

Claim 61 (withdrawn): A method as set forth in claim 60 wherein said microorganisms are selected from the group comprising infectious bursal disease virus and chicken anemia virus.

Claim 62 (withdrawn): A method as set forth in claim 59 wherein said sterilization is by a chemical disinfectant other than an alkali metal dichromate.

Claim 63 (withdrawn): A method as set forth in claim 59 wherein said chemical disinfectant comprises a solution of an alkali metal hypochlorite.

Claim 64 (withdrawn): A method as set forth in claim 63 wherein said chemical disinfectant comprises a solution of sodium hypochlorite.

Claim 65 (withdrawn): A method as set forth in claim 64 wherein said solution used is at a concentration from about 1% to about 20% by volume of active chlorine.

Claim 66 (withdrawn): A method as set forth in claim 65 wherein said is at a concentration from about 5% to about 15% by volume of active chlorine.

Claim 67 (withdrawn): A method as set forth in claim 66 wherein said solution is at a concentration of about 10% by volume of active chlorine.

Claim 68 (withdrawn): A method as set forth in claim 64 wherein said sporulated oocysts are treated with said sodium hypochlorite from about 5 to about 25 minutes.

Claim 69 (withdrawn): A method as set forth in claim 68 wherein said sporulated oocysts are treated with said sodium hypochlorite from about 8 to about 20 minutes.

Claim 70 (withdrawn): A method as set forth in claim 69 wherein said sporulated oocysts are treated with said sodium hypochlorite for about 10 minutes.

Claim 71 (withdrawn): A method as set forth in 63 further comprising substantially separating said sodium hypochlorite from the sporulated oocysts by filtration.

Claim 72 (withdrawn): A method as set forth in claim 71 wherein said filtration is by means of tangential flow filtration.

Claim 73 (withdrawn): A method for inducing sporulation of oocysts comprising:

introducing into an aqueous sporulation medium oocysts of at least one species of protozoa known to cause coccidiosis;

incubating said oocysts in said aqueous sporulation medium, thereby causing sporulation of oocysts; and

introducing an oxidizing agent having a standard reduction potential of at least about 0.5 V into said medium at a rate sufficient to maintain the oxidation potential of said medium equivalent to the oxidation potential of a medium containing dissolved molecular oxygen in concentration of at least 30% of saturation during sporulation;

said medium containing less than about 0.8% by weight alkali metal dichromate during incubation of said oocysts.

Claim 74 (withdrawn): A method for sporulating oocysts comprising:

introducing into an aqueous sporulation medium oocysts of at least one species of protozoa known to cause coccidiosis;

incubating said oocysts in said aqueous sporulation medium, thereby causing sporulation of oocysts; and

separating said oocysts by tangential flow filtration from said sporulation medium.

Claim 75 (withdrawn): A method for sterilizing oocysts comprising:

contacting oocysts of at least one species of protozoa known to cause coccidiosis with a sterilization medium; and

removing said sterilization medium from said oocysts by tangential flow filtration.

Claim 76 (withdrawn): A method for monitoring sporulation of oocysts comprising:

incubating viable oocysts in an aqueous sporulation medium; and

during incubation, monitoring said medium to detect a change in at least one of the following parameters:

(i) dissolved oxygen content;

(ii) pH;

(iii) rate of introduction of oxidizing agent into said medium;

(iv) flow rate of acid or base into said medium.

Claim 77 (withdrawn): A method as set forth in claim 76 wherein dissolved oxygen content of said medium is controlled by addition of molecular oxygen thereto, and monitoring sporulation comprises detecting a change in oxygen consumption as indicated by detection of a change in oxygen flow to the medium and/or a permanent or transient change in dissolved oxygen content.

Claim 78 (withdrawn): A method as set forth in claim 76 wherein pH of said medium is controlled by addition of acid or base thereto, and monitoring sporulation comprises detecting an increase in acid consumption as indicated by an increase in acid flow to the medium and/or a permanent or transient increase in pH.

Claim 79 (withdrawn): A method as set forth in claim 76 wherein the end point of sporulation is determined from substantial cessation of oxygen consumption or generation of alkalinity in the sporulation medium.

Claim 80 (withdrawn): A method as set forth in claim 79 wherein the end point is indicated by the substantial cessation of change in at least one of said parameters.

Claim 81 (withdrawn): A method as set forth in claim 79 wherein said sporulated oocysts are maintained is said medium under sporulation conditions for at least another 48 hours after the indicated end point of sporulation.

Claim 82 (withdrawn): A method as set forth in claim 76 wherein said change in dissolved oxygen content is a decrease.

Claim 83 (withdrawn): A method as set forth in claim 76 wherein said change in pH is an increase.

Claim 84 (withdrawn): A method as set forth in claim 83 wherein said increase in pH is at least 0.5 pH units.

Claim 85 (withdrawn): A method as set forth in claim 84 wherein said increase in pH is at least 0.25 pH units.

Claim 86 (withdrawn): A composition for the storage of sporulated oocysts comprising an aqueous diluent and a bactericide, said composition characterized as substantially free of alkali metal dichromate wherein said composition is characterized as having:

a diluent comprising 0.5X phosphate buffered saline;

a pH from about 5.0 to about 8.0; and

wherein said bactericide is selected from the group consisting of an alkali metal perchlorate, an alkali metal hypochlorite, hydrochlorous acid, sodium hydroxide and antibiotics.

Claim 87 (withdrawn): A composition as set forth in claim 86 having a pH from about 7.0 to about 7.5.

Claim 88 (withdrawn): A composition as set forth in claim 86 wherein said bactericide comprises gentamicin.

Claim 89 (withdrawn): A composition as set forth in claim 86 further comprising an oxidizing agent.

Claim 90 (withdrawn): A composition as set forth in claim 86 characterized in that an oocyst population in contact with said composition remains at least about 60% viable for 13 weeks at about 25° C.

Claim 91 (withdrawn): A composition as set forth in claim 86 characterized in that an oocyst population in contact with said composition remains at least about 60% viable for 26 weeks at about 5°C.

Claim 92 (withdrawn): A composition as set forth in claim 86 characterized in that an oocyst population in contact with said composition decrease in viability no more than about 20% over a period of at least about 13 weeks at about 25°C.

Claim 93 (withdrawn): A composition as set forth in claim 86 characterized in that an oocyst population in contact with said composition decrease in viability no more than about 20% over a period of at least about 26 weeks at about 5°C.

Claim 94 (withdrawn): A composition as set forth in claim 86 further comprising a dye.

Claim 95 (withdrawn): A composition for the storage of sporulated oocysts comprising:

0.5X PBS; and

about 30 µg/ml gentamicin,

said composition characterized as substantially free of alkali metal dichromate, and wherein said composition is characterized in that oocysts in contact with said composition decrease in viability no more than about 20% over a period of at least about 26 weeks at about 5°C.

Claim 96 (withdrawn): A method for storing sporulated oocysts comprising contacting said sporulated oocysts with the composition of claim 86.

Claim 97 (withdrawn): A method as set forth in claim 96 further comprising storing said sporulated oocysts in contact with the composition of claim 86 at either about 25°C or about 5°C.

Claim 98 (withdrawn): A method as set forth in claim 96 wherein said population of sporulated oocysts is maintained at least 60% viable for 13 weeks at about 25°C.

Claim 99 (withdrawn): A method as set forth in claim 96 wherein said population of sporulated oocysts is maintained at least 60% viability for 26 weeks at about 5°C.

Claim 100 (withdrawn): A method as set forth in claim 96 wherein said method prevents a decrease in oocyst viability of greater than 20% over a period of at least 13 weeks at about 25°C.

Claim 101 (withdrawn): A method as set forth in claim 96 wherein said method prevents a decrease in viability of greater than 20% in a population of sporulated oocysts over a period of at least 26 weeks at about 5°C.

Claim 102 (previously presented): The method of claim 6 wherein the dense aqueous liquid is selected from the group consisting of sucrose and fructose corn syrup.

Evidence Appendix to Appeal Brief Under Rule 47.37(c)(1)(ix)

A copy of Dr. Knight's and Dr. Dibner's Declaration under 37 C.F.R. § 1.132 was initially submitted to the USPTO on August 3, 2009, as part of the response to the non-final Office Action mailed June 24, 2009. The response was entered by the Examiner as indicated by the Final Action mailed October 28, 2009. Dr. Knight's and Dr. Dibner's previously submitted declaration also included a copy of their curricula vitae, demonstrating their collective knowledge and expertise in the technical field. A copy of the Declaration, as previously submitted, is hereby attached as evidence to the Appeal Brief.

Related Proceedings Appendix to Appeal Brief Under Rule 47.37(c)(1)(x)

There are no related decisions for this appeal.

PATENT
Attorney Docket No.: 048968-117958
Via EFS-Web

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	Group Art Unit: 1645
SCHASTEEN *et al.*	)	
	)	
Application No.: 10/799,083	)	Examiner: Vanessa L. Ford
	)	
Filed: March 12, 2004	)	
	)	Confirmation No. 8520
For: METHODS AND COMPOSITIONS FOR THE CONTROL OF COCCIDIOSIS	)	

EVIDENCE APPENDIX

PATENT
Atty. Docket No. 048968-117958
Via EFS-Web

UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Schasteen *et al.*	Art Unit	1645
Serial No.:	10/799,083	Examiner:	Vanessa Ford
Filed:	March 12, 2004	Conf. No.	8520
For:	METHODS AND COMPOSITIONS FOR THE CONTROL OF COCCIDIOSIS		

DECLARATION OF CHRISTOPHER D. KNIGHT AND JULIA J. DIBNER

UNDER 37 C.F.R. § 1.132

Christopher D. Knight, Ph.D., and Julia J. Dibner, Ph.D., declare and state as follows:

1. I, Christopher D. Knight, have over twenty years of experience in the field of animal health and nutrition. Novus International Inc., a global leader in animal health and nutritional products, currently employs me as Vice-President for Research and Development. My employment by Novus International has been continuous for over seventeen years. Prior to my employment at Novus International Inc., I was employed by Monsanto in their Animal Sciences Division for over five years. My educational background includes a Bachelor of Science degree in Animal science awarded by Cornell University in 1975; a Master of Science degree in Monogastric Nutrition awarded by Purdue University in 1977; and a doctorate degree (*i.e.*, Ph.D.) in Monogastric Nutrition awarded by Purdue University in 1981. I have also published over approximately thirty journal articles or posters at internationally attended meetings, and I am an inventor on ten patents. Attached to this Declaration is a copy of my curricula vitae.

2. I, Julia J. Dibner, have over twenty years of experience in the field of animal health and biological sciences. Novus International Inc., a global leader in animal health and nutritional products, currently employs me as a Senior Scientist and Distinguished Fellow. My employment by Novus International has been continuous for over seventeen years. Prior to my employment at Novus International Inc., I was employed by Monsanto in their Animal Sciences Division for approximately ten years. My educational background includes a Bachelor of Arts degree in Biology and Anthropology awarded by the State University of New York at Binghamton; a Research Fellowship in Biochemistry at the State

University of New York at Binghamton; and a doctorate degree (*i.e.*, Ph.D.) in Cellular and Developmental Biology awarded by Washington University in St. Louis. I have also published over approximately ninety journal articles or posters at internationally attended meetings, and I am an inventor on seven patents. Attached to this Declaration is a copy of my curricula vitae.

3. We, Christopher D. Knight and Julia J. Dibner, identified as above, have reviewed and are familiar with U.S. Patent Application Publication No. 2004/0175391 (the '391 application; U.S. Serial No. 10/799,083) entitled "Methods and Compositions for the Control of Coccidiosis." The '391 application has claims directed toward methods for isolating viable oocysts with a hydrocyclone. The claimed oocyst/hydrocyclone technology is presently utilized by Novus International Inc. in the making of the ADVENT® Coccidiosis Control product, which is an orally applied coccidiosis live-vaccine that offers a number of advances within the field, including the elimination of hazardous chemicals in the vaccine.

4. Through our employment at Novus as indicated above, we both are familiar with and have supervised portions of the research and development efforts that resulted in the discovery of the methods currently claimed in the '391 application. At the outset of the project, we were skeptical that hydrocyclones could be used to isolate viable oocysts. To be useful for the production of a live-vaccine, the oocysts are required to be viable following isolation. Oocysts, however, were known in the art to be extremely fragile and destroyed by agitation, stirring, or even by the mechanical action of digestion. See, *e.g.*, newly identified supporting references showing the general state of the art, including U.S. Patent No. 4,808,404 ("The sporozoites of *Elimeria* species once out of their protective shells, *i.e.*, oocysts and sporocysts, are very fragile and lose their infectivity within a few days."); U.S. Patent No. 6,891,024 ("Oocysts and sporocysts are found in the intestinal contents but the fragile oocyst is commonly disrupted by the time feces are passed."); and U.S. Patent No. 6,998,126 ("The wall of the sporulated oocyst is ruptured by the mechanical action in the gizzard and intestinal tract . . ."). Our experience at Novus International in handling oocysts further confirms that they are extremely fragile and subject to rupture.

5. Thus, in the initial stages of the project resulting in the '391 application, we were skeptical that a hydrocyclone could be used to isolate a viable oocyst since hydrocyclones apply extreme sheer forces, which we thought were likely to destroy the oocysts. Hydrocyclones had not been previously used to isolate oocysts. At the time, our only knowledge of the use of hydrocyclones was for the removal of waste products, for example, in mining or other industrial applications. There were no positive indications

for using a hydrocyclone to separate oocysts, particularly when the oocysts needed to be viable.

6. In the recent Office Action concerning the '391 application, mailed on June 24, 2009, the Patent Office cites to a new reference referred to as Alesina *et al.* (SU 19984621763; "Alesina"). The abstract provided of Alesina refers to a hydrocyclone for use in microorganism suspension separation. The reference, however, makes no mention whether the microorganism suspension would be live or dead before or after separation. Furthermore, the term "microorganism" is not an art-recognized equivalent of oocysts, since oocysts are more akin to fertilized eggs, which are not yet developed enough to be infective. Physically, oocysts are also much larger and less dense than microorganisms such as bacteria, including structural differences in the outer membrane/cell wall that make oocysts substantially more fragile than bacteria. Consequently, oocysts would not be considered to be the same or substantially similar to the term "microorganisms" as set forth by the Patent Office.

7. The Office Action further states at page 7 that Conkle *et al.* " . . . suggest the use of other methods of processing oocysts to eliminate the use of harsh chemicals such as potassium dichromate." This is not technically correct, first, because Conkle still uses potassium dichromate as an oxidizing agent at page 8, line 6 of Conkle, such that potassium dichromate would still be present in their vaccine. Secondly, and more importantly, potassium dichromate is used for its biostatic/oxidizing ability (*i.e.*, to minimize bacterial growth within the remaining fecal matter), not for oocyst isolation. There is no relationship between potassium dichromate and new methods of separation/isolation. Thus, there is no relationship between potassium dichromate and the use or non-use of a hydrocyclone. Rather, as mentioned previously, there were a number of factors that made us initially believe that using a hydrocyclone would not be effective at isolating a viable oocyst for making a live-vaccine.

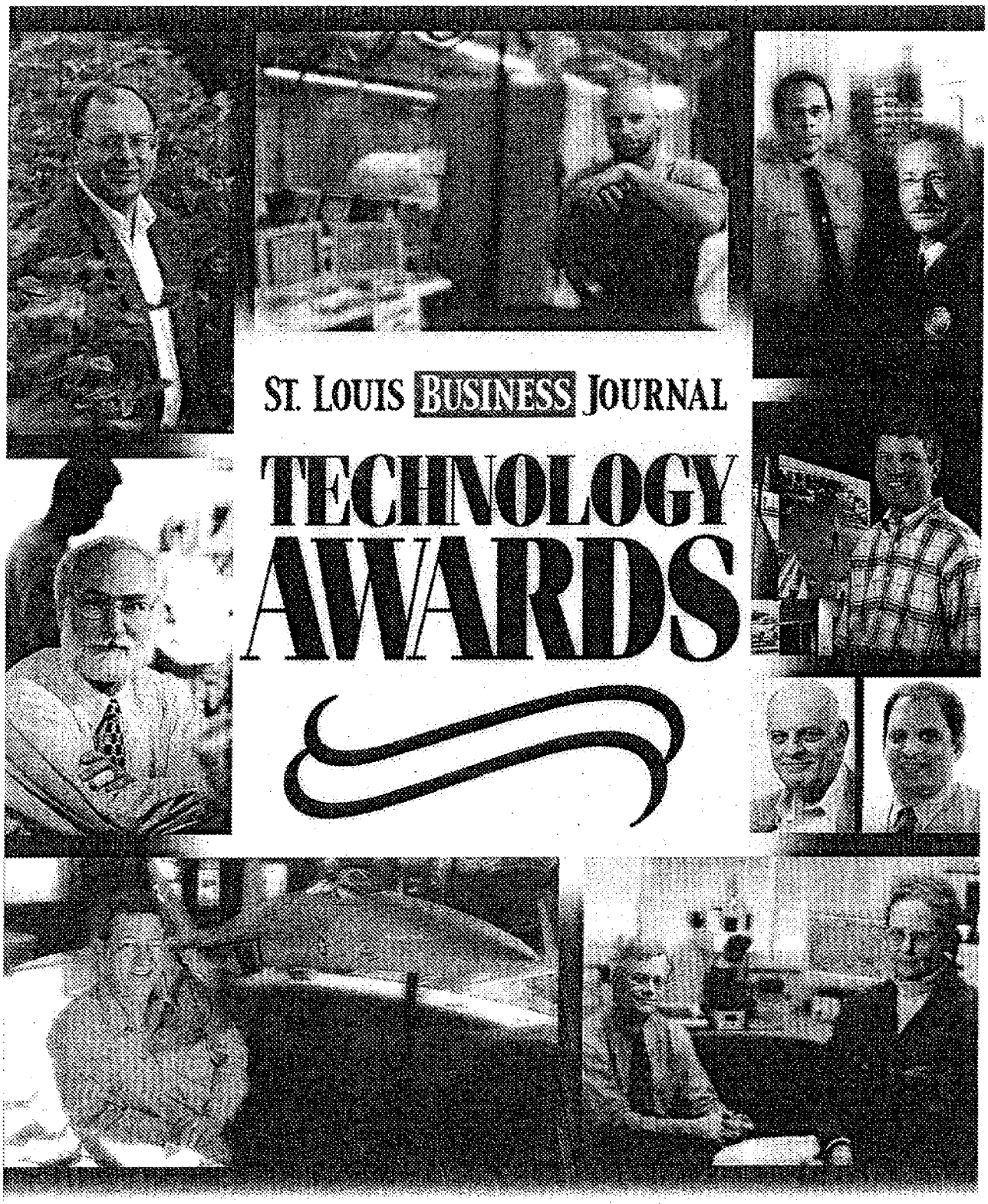
8. There were also additional obstacles that were overcome in arriving at the '391 application that may be worthy of consideration. Since the oocysts and the slurry particles from which the oocysts were isolated were of similar densities, it was difficult to find the appropriate pressure parameters that would allow effective isolation and not destroy the oocysts in the hydrocyclone. At the outset of the project, it appeared that any pressure that allowed separation of the oocyst from the slurry particles would also destroy the oocysts. The appropriate pressure conditions were ultimately discovered, however, and are fully described in the '391 application specification.

9. As a matter of general interest, we have also attached to this declaration a copy of an article from the St. Louis Business Journal, published in April of 2003. The Business Journal article identifies us, Christopher D. Knight and Julia J. Dibner, as St. Louis Technology Award recipients for our contributions in developing the ADVENT® vaccine, which is used to treat coccidiosis in poultry.

10. We further declare that all statements made herein are of our own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Christopher D. Knight, Ph.D. — Date: 7/31/2009

Julia J. Dibner, Ph.D. — Date: 8/3/09



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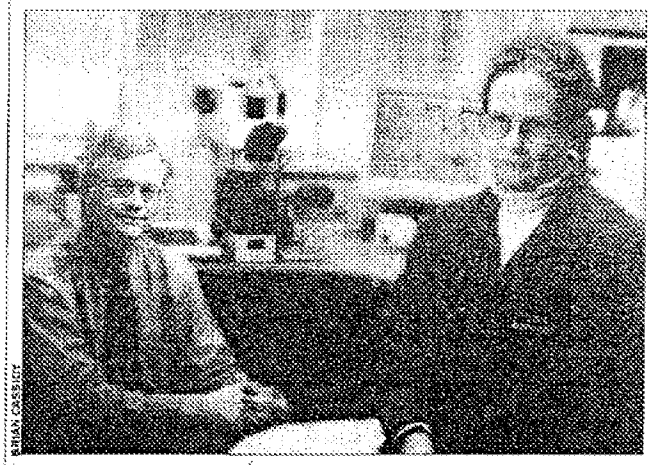

BRIAN CASSELLY

Chris Knight and Julia Dibner have spent five years developing a coccidiosis vaccine.

CHICKEN CURING

Scientists at Novus develop vaccine to treat No.1 poultry threat

BY CHAD GARRISON
cgarrison@bjournals.com

Chicken producers the world over may soon be praising the names of Chris Knight and Julia Dibner, scientists with the animal agricultural firm Novus International Inc.

Last December, Knight, head of research and development for Novus, and Dibner, a senior scientist with the company, received USDA approval for Advent, a new vaccine they developed for the treatment of coccidiosis in broiler chickens. Coccidiosis, a potentially deadly parasitic protozoa, is estimated to cost the world's poultry producers some $700 million in annual losses, according to industry publications.

In the United States, the highly contagious coccidiosis is the No. 1 threat for poultry producers, who spend between $60 million and $70 million annually on drugs designed to prevent chickens from catching the disease, according to the USDA.

Currently, some 90 percent of broiler chickens (those used primarily for food sources) are treated for coccidiosis through drugs and chemicals placed in their feed. Knight's and Dibner's vaccine, on the other hand, is sprayed onto young chicks a day after they are hatched. This biological treatment, in which the chicks are exposed to a non-threatening form of coccidiosis, causes the animals to develop natural antibodies that render them immune from the disease.

The two scientists, who have worked together for nearly 28 years (first at Monsanto and then Novus), spent the past five years working on the vaccine. Unlike the few other coccidiosis vaccinations for broiler chickens, Advent takes advantage of technology developed by Novus that allows scientist to accurately measure the number of living organisms within the vaccine: an important step in determining the vaccine's potency. Furthermore, the strict manufacturing process of the vaccine guarantees its purity.

Tim Cherry, a professor of poultry science at Stephen F. Austin State University in Nacogdoches, Texas, who has spent the past 13 years studying and researching coccidiosis, said the Advent vaccine is far more consumer- and producer-friendly than current methods of preventing the disease.

"There are two main concerns currently surrounding the traditional prevention methods of treating coccidiosis: resistance of the organism to drugs and the worldwide consumer preference for animals to be fed less drugs and chemicals," he said. "Advent addresses both of those issues because with the vaccine drug resistance is not a factor and you don't have to use drugs or chemicals in the feed."

Currently, Advent is being tested by nearly all the major poultry producers in the United States, and Knight and Dibner are confident its use will gain popularity once producers realize its efficiency and reliability.

Of the 8.5 billion broiler chickens produced annually in the United States, only 7 percent to 8 percent of those birds are treated for coccidiosis through vaccinations, Knight said.

Novus International Inc., had sales of $406 million last year. The company, headquartered in Maryville Center, with a research facility in St. Charles, was originally the Animal Feed Ingredients division of Monsanto Co. In 1991, the division was spun off from Monsanto and purchased by a Japanese joint venture.

CURRICULUM VITAE

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Education

1977-1981	Ph.D. in Monogastric Nutrition Purdue University, West. Lafayette, IN Department of Animal Science. Graduate Instructor, 1977-1981
1975-1977	M.S. in Monogastric Nutrition Purdue University, West. Lafayette, IN Department of Animal Science. Graduate Research Assistant
1973-1975	B.S. Animal Sciences Cornell University, Ithaca, NY
1971-1973	A.A.S. Science Laboratory Technology State University of New York at Cobleskill

Employment

2006-Present	Vice-President, Research & Development Novus International, Inc.
2001-2006	Department Head, Research & Development Novus International, Inc.
1996-2001	Director New Business Development Novus International, Inc.
1991-1995	Manager and Director Nutrition Research Novus International, Inc
1987-1991	Research Group Leader Monsanto Company Animal Sciences Division Porcine Somatotropin Group
1981-1986	Research Specialist and Research Group Leader Monsanto Co: Alimet Metabolism and Applications Research Group

Key Accomplishments

- Developed and implemented a Novus International sponsored Graduate Scholarship program outside the U.S. to support graduate students in animal nutrition and health, and to develop a technical network of expertise that Novus can collaborate with in our basic and applied approach to product development and problem solving. This program allows us to encourage an international perspective to you graduates in animal agriculture as well as introduce the research based approach of Novus in world areas where Novus in expanding. This program began in 2006 in China and involves 8 different agriculture universities and provides 32 scholarships per year in addition to 8 internships to the US each year. Both Purdue University and University of Missouri-Columbia work collaboratively with Novus in the execution of certain aspects of this program. In 2008, we have expanded this program to include Pukyang National University, in Pusan Korea, specializing in Aquaculture and supporting 3 graduate students per year; and Bombay Veterinary College, Mumbai, India supporting one student per year in mineral metabolism. This program involves annual visits and joint university and industry seminars each year to facilitate industry and academic interaction and sharing of research. In each case, this program has been the first of its kind in each of these universities and offers a unique approach to industry and academic collaboration.

- Developed foundation data quantifying availability of ALIMET® Feed Supplement as a rumen-available and rumen by-pass methionine source in lactating dairy cattle and methods to predict methionine deficiency using existing nutritional models. These data resolved decades of research work to attempting to commercialize this product application that had failed due to unpredictable field results. The research demonstrated Alimet to be the most cost-effective source of post-ruminal methionine activity available, resulted in a US patent and the development of a $5M/yr business for Novus. As of 2005, a new Ruminant Business Unit has been formed with 20 employees and agents and a portfolio of 8 products (including Alimet and MHA) for the dairy industry. Sales in FY08 were $20M.

- Led the development and commercialization of OASIS® Hatchling Supplement, a hydrated nutritional supplement fed to young poultry in transit or to stimulate rapid onset of ad libitum feeding after placement. This patented product developed a new market in the poultry industry based on developmental research at Novus showing the impact of early nutrition on subsequent long term performance and health. Cumulative sales of this niche product have exceeded $5M and resulted in the development of gastrointestinal health as a core research and development competency within Novus.

- Led the technology development, regulatory approval and early commercialization of ADVENT® Coccidiosis Control, an orally applied coccidiosis vaccine based upon technology that permits the in vitro determination of oocyst viability such that a vaccine of consistent potency can be produced and marketed. This represented a new area of

technology for Novus and in 2003, a jury of scientists and technology experts from Washington University and St. Louis University awarded the developers of this technology (Dr. Julia Dibner and Dr. Chris Knight) with The St. Louis Technology Award. The Advent Coccidiosis Control technology was among eight other winners from approximately 70 nominations in the St. Louis vicinity. In determining winners, the judges considered the scope, economic impact and overall significance of the new technology. Facilitated by the Academy of Science of St. Louis, the judging process also examined the level of sophistication of the entries and the innovation utilized to bring it to fruition. This technology represents a keystone of a business strategy that focuses on gastrointestinal health and drug-free poultry production.

- In 2007, successfully developed a low pathology strain of E. tenella that resulted in robust immunity with reduced lesion production in the bird and better subsequent production. This allowed for a re-introduction of Advent in the US market that has allowed for a significantly expanded market penetration of the vaccine and provided intellectual property to protect the selection process used to develop the strain.

- Established a new cost-efficient method of product development research, to insure Novus' capability to conduct scientifically and commercially relevant research across multiple species without requiring ownership or hands on care and management of research facilities. Initially divested Novus-owned animal research facilities and sought collaborative investment opportunities with scientific professionals in animal agriculture to provide capital for research facilities that would be controlled by the research partner but provide Novus with preferred status for conduct of research. To date we have formed 3 partnerships like this in the US that permits routine product development work in broilers, swine (weaning, grow-finish and lactating sows) and dairy cattle, all in commercial scale production environments. Similar agreements are under development in Brazil (commercial scale broiler research) and China (commercial scale swine research including wean, grow-finish and sow nutrition).

- The foundation product for Novus International is ALIMET® Feed Supplement, a source of methionine activity referred to as methionine hydroxyl analog or chemically DL-2-hydroxy-4-(methylthio) butanoic acid. Today this business represents approximately $700M in annual revenue to Novus in a $2B methionine market, however, in 1981 this represented about a $20M business. In the course of my 25 year involvement with this product there has been a heated commercial controversy with respect the relative efficacy of Alimet and the competitive product DL-methonine (DLM). A close colleague (Dr. Julia Dibner) and I have had the responsibility of understanding the absorption, metabolism and utilization of Alimet, how it differs from that of DLM and the impact that the differences have on the commercial value of Alimet relative to DLM. Today based on a variety of independent and collaborative research efforts it is understood that the metabolism of Alimet is very different from DLM, that those differences result in differences in ad libitum feed intake (less than DLM at low supplementation rates, greater than DLM at the maximum response level) resulting in different dose responses for the two methionine sources. A substantial part

of the controversy was based on the a priori assumption that the two products must have the same dose response since they both provide methionine. With collaboration with various statistical experts, we have been able to establish that the two products in fact have different dose responses and have described the appropriate statistical methods for comparing two products that exhibit different dose responses (Poult. Sci. 85:947-954). The controversy will continue due to commercial conditions (Alimet is less expensive to manufacture than DLM) , however over the course of 25 years Alimet has continued to grow at a 25% compounded annual growth rate with over a 50% market share in the US. The science applied to this commercial issue has laid the technical foundation that has provided Novus with the technical credibility to expand our product offerings from amino acids into nutritional organic acid blends, organic trace minerals, ingredient preservation and coccidiosis control.

Personal

- Married 1982: Sandra J. Rogers (Purdue Food Science MS 1978).
- Children: Adam (22), Evan (19), Audrey (18)

Community involvement

- Subdivision Trustee: 1987-1989: Led resolution of road and storm sewer repair dispute
- St. Peter's Episcopal Church:
    - Youth Sponsor: 1984-1988
    - Sunday School Teacher:1992-2006 (Variety of grades and curricula)
    - Vestry: 1989-1993
    - Founding Christian Education Commission & Chair: 1989-1993
    - Confirmation Teacher: 2005-6.
    - Founding and sustaining member of Haven of Grace: Home for unwed mothers
- Hobbies
    - Cooking
    - Gardening
    - Kid's Sports

Professional Societies & Honors

- American Society of Animal Science
- Poultry Science Association
- 2003 St. Louis Technology Award for Advent Coccidiosis Control development
- 2007 Distinguished Alumni Award Purdue Department of Animal Science
- 2009 Distinguished Alumni Purdue School of Agriculture Award

PUBLICATIONS & PROCEEDINGS

1. Dibner, J.J. and **C.D. Knight** (1984) Conversion of 2-hydroxy-4-(methylthio) butanoic acid to L-methionine in the chick: A stereospecific pathway. J. Nutr. 114:1716-1723.

2. **Knight, C.D.** and J.J. Dibner (1984) Comparative absorption of 2-hydroxy-4-(methylthio)butanoic acid and L-methionine in the broiler chick. J. Nutr. 114:2179-2186.

3. Dibner, J.J., F.J. Ivey, C.Q. Lawson and **C.D. Knight** (1986) In *vitro* methods in animal nutrition. Proceedings of the Conference European D'Aviculture 7:312-316.

4. Dibner, J.J., **C.D. Knight**, R.A. Swick and F.J. Ivey (1987) Absorption of 2-hydroxy-4-(methylthio) butanoic acid from the hindgut of the broiler chick. Poult. Sci. 67:1314-1321.

5. Dibner, J.J., **C.D. Knight**, C.Q. Lawson, R.A. Swick and F.J. Ivey (1990) Studies of the metabolism of 2-hydroxy-4-(methylthio)butanoic acid (HMB, Alimet®) in the broiler chick using *in vitro* methods. Memorias: XI Congreso de Avicultura Centroamericano y del Caribe, pp15-18.

6. **Knight, C.D.**, J.J. Dibner and F.J. Ivey (1991) Crystalline amino acid diets for chicks: History and future. Maryland Nutrition Conference Proceedings pp 19-28.

7. **Knight C.D.**, Kasser T.R., Swenson G.H., Hintz R.L., Azain M.J., Bates R.O., Cline T.R., Crenshaw J.D., Cromwell G.L., Hedrick H.B. 1991. The performance and carcass composition responses of finishing swine to a range of porcine somatotropin doses in a 1-week delivery system. J. Anim. Sci. 69:4678-89.

8. Collier R.J., Vicini J.L., **Knight C.D.**, McLaughlin C.L., Baile C.A. 1992. Impact of somatotropins on nutrient requirements in domestic animals. J. Nutr. 12293 Suppl):855-60.

9. Becker B.A., **Knight C.D.**, Veenhuizen J.J., Jesse G.W., Hedrick H.B. Baile CA.1993. Performance, carcass composition, and blood hormones and metabolites of finishing pigs treated with porcine somatotropin in hot and cold environments. J Anim Sci.71:2375-87.

10. Becker. B. A., **C.D. Knight**, F.C. Buonomo, G.W. Jesse, H.B. Hedrick, C. A. Baile. 1992. Effect of a hot temperature environment on performance, carcass characteristics, and blood hormones and metabolites of pigs treated with porcine somatotropin. J. Anim. Sci. 70: 2732-40.

11. Ledoux, D.R., **C. D. Knight**, B. A. Becker and C.A. Baile. 1993. Effects of a porcine somatotorpin implant on tissue mineral status of finishing pigs exposed to a thermoneutral or cold environment. J. Anim. Sci. 1993. 71:2180-2186.

12. **Knight, C.D.**, C.W. Wuelling, C.A. Atwell and J.J. Dibner. 1994. Effect of Intermittent Periods of High Environmental Temperature on Broiler Performance Responses to Sources of Methionine Activity. Poultry Science 73:627-639.

13. Hammond B.G., Vicini J.L., Hartnell G.F., Naylor M.W., **Knight C.D.**, Robinson E.H., Fuchs R.L., Padgette S.R. 1996. The feeding value of soybeans fed to rats, chickens, catfish and dairy cattle is not altered by genetic incorporation of glyphosate tolerance. J Nutr. 1996. 126(3):717-27.

14. **Knight, C.D.**, C.A. Atwell. C.W. Wuelling, F.J. Ivey and J.J. Dibner, 1998. The relative effectiveness of 2-hydroxy-4-(methylthio) butanoic acid and DL-methionine in young swine. J. Anim. Sci. 76:781-787.

15. Dibner, J.J., F.J. Ivey, and C.D. Knight. 1998. The feeding of neonatal poultry. World Poultry, No. 5, Vol. 14: 36-40.

16. Dibner, J.J., **C.D. Knight**, M.L. Kitchell, C.A. Atwell A.C. Downs and F.J. Ivey, 1998. Early feeding and development of the immune system in neonatal poultry. J. App. Poult. Res. 7:425-436.

17. Dibner, J.J., F.J. Ivey and **C.D. Knight**, 1999. Direct delivery of live coccidiosis vaccine into the hatchling yolk sac. World Poultry-Coccidiosis Special p. 28-29.

18. Koenig K.M., L. M. Rode, **C. D. Knight**, and P. R. McCullough. 1999. Ruminal escape, gastrointestinal absorption, and response of serum methionine to supplementation of liquid methionine hydroxyl analog in Dairy cows. J. Dairy Sci. 82:355-361.

19. Dibner, J.J., and **C.D. Knight**. 2001. Early Feeding and Nutritional Programming in Hatchling Poultry. Proceedings Arkansas Nutrition Conference, Sept. 11-13.

20. Koenig K.M., M. Vázquez-Añón, **C. D. Knight**, and L. M. Rode. 2002. Ruminal escape and response of serum methionine to 25 and 50 grams of methionine hydroxy analog in dairy cows. J. Dairy Sci. 85:930

21. Dibner, J.J. and **C.D. Knight**, 2003. Early nutrition and immune development. Proceedings: California Animal Nutrition Conference, pp. 172-178. Fresno, CA, May 13 & 14, 2003.

22. Dibner, J.J., and **C.D. Knight**. 2003. Early Nutrition: Effect of feed and water on livability and performance. Proceedings: 27th North Carolina Turkey Industry Days. pp 12- 17.

23. Dibner, J.J., M.A. Pfannenstiel, M.L. Kitchell and **C.D. Knight**, 2003. Importance of viability testing for coccidiosis vaccines. World Poultry-Coccidiosis Special p. 11-12.

24. Dibner, J.J., M.A. Pfannenstiel, J.K. McMillen, J. Green, and **C.D. Knight.** 2003. Safety and Efficacy of a high definition coccidiosis vaccine. Proceedings of the Fifty-Second Western Poultry Disease Conference, March 8-11. pp 83-86.

25. Vazquez-Anon, M., M. Wehmeyer, T. Hampton, **C.D. Knight** and J.J. Dibner, 2003. Differential response to 2-hydroxy-4-(methylthio) butanoic acid and DL-methionine above requirements on broiler and pig performance and iron metabolism., EEAP Publication 109: Progress in Research on Energy and Protein Metabolism, pg. 725-729.

26. Dibner, J.J., M. Quiroz, S.J. Mueller and **C.D. Knight**, 2004. Recent developments in broiler coccidiosis control: Comparison of vaccination with coccidiostats in broilers on used litter. Zootecnica International, March, 2004: 44-49.

27. Dibner, J.J., M. Vazquez-Anon, David Parker, Ricardo Gonzalez-Esquerra and **C.D. Knight**, 2004. Use of Alimet® Feed Supplement (2-hydroxy-4-methylthio butanoic acid, HMBTA) for broiler production. Japanese J. Poultry Sci., 41:214-223.

28. Gaines A.M., Yi G.F., Ratliff B.W., Srichana P., Kendall D.C., Allee G.L., **Knight C.D.**., Perryman K.R. 2005. Estimation of the ideal ratio of true ileal digestible sulfur amino acids:lysine in 8- to 26-kg nursery pigs. J Anim. Sci.83:2527-34.

29. Vázquez-Añón, M. D. Kratzer, R. González-Esquerra, I. G. Yi, and **C. D. Knight**. 2006. A Multiple Regression Model Approach to Contrast the Performance of 2-Hydroxy-4-Methylthio Butanoic Acid and DL-Methionine Supplementation Tested in Broiler Experiments and Reported in the Literature. Poult. Sci. 85: 693-705.

30. Vázquez-Añón, M., R. Gonzalez-Esquerra, E. Saleh, T. Hampton, S. Richter, J. Firman, and **C. D. Knight**. 2006. Evidence for 2-Hydroxy-4-Methylthio Butanoic Acid and DL-methionine having a Different Dose-Response in Growing Broilers. Poult. Sci. 85:1409-1420.

31. **Knight,C.D.**, J. J. Dibner, R. Gonzalez-Esquerra, and M. Vázquez-Añón. 2006. Differences in broiler growth rates when methionine (MET) sources are fed in deficiency or excess are equalized when feed consumption is equalized. Poul. Sci. 85 (Suppl. 1): P191 (Abstr.)

32. G. F. Yi, A. M. Gaines, B. W. Ratliff, P. Srichana, G. L. Allee, K. R. Perryman, and **C. D. Knight**. 2006. Estimation of the true ileal digestible lysine and sulfur amino acid requirement and comparison of the bioefficacy of 2-hydroxy-4-(methylthio)butanoic acid and DL-methionine in 11- to 26-kg nursery pigs. J. Anim. Sci. 84: 1709-1721.

33. J. D. Richards and **C. D. Knight** (2007). Organic trace minerals bioavailability and functional effects in animals. Chinese Association of Animal Science and Veterinary Medicine Proceedings of the Second National Symposium on Poultry Nutrition and Feed Science, Beijing, China, September 10-11, 2007, pp. 341-344.

34. G. F. Yi, C. A. Atwell, J. A. Hume, J. J. Dibner, **C. D. Knight** and J. D. Richards (2007). Determining the Methionine Activity of MINTREX® Organic Trace Minerals in Broiler Chicks by Using Radiolabel Tracing or Growth Assay. Poultry Sci.86:87-887.

35. Richards, J.D., J.J. Dibner, and **C.D. Knight**. 2007. REPLY: 2-Hydroxy-4(Methylthio) butanoic acid from any commercial source is fully available as a source of methionine activity. Poultry. Sci. 86:1613-1614.

Patents

1. U.S. 6,814,988 – Process for optimizing milk production.

2 U.S. 6,733,759 – Nutrient formulation and process for enhancing the health, livability, cumulative weight gain or feed efficiency in poultry and other animals.

3 U.S. 6,329,001 – Nutrient formulation and process for enhancing the health, livability, cumulative weight gain or feed efficiency in poultry and other animals.

4 U.S. 6,319,525 – Process for optimizing milk production.

5 U.S. 6,210,718 – Nutrient formulation and process for enhancing the health, livability, cumulative weight gain or feed efficiency in poultry and other animals.

6 U.S. 6,183,786 – Process for optimizing milk production.

7 U.S. 6,017,563 – Process for optimizing milk production.

8 U.S. 5,985,336 – Nutrient formulation and process for feeding young poultry and other animals.

9 U.S. 5,976,580 – Nutrient formulation and process for enhancing the health, livability, cumulative weight gain or feed efficiency in poultry and other animals.

10 U.S. 5,928,686 – Nutrient formulation and process for feeding young poultry and other animals.

CURRICULUM VITAE

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Education

1976-1980	Ph.D. in Cellular and Developmental Biology Washington University, St. Louis Division of Biology and Biomedical Sciences. Graduate Fellowship, 1976-1980
1972-1975	Doctoral student in Biochemistry State University of New York at Binghamton Research Fellowship, 1974-1975 Graduate Assistant, 1972-1974
1969-1972	B.A., Summa cum laude, June, 1972 State University of New York at Binghamton Majors in Biology and Anthropology

Employment

2004-	Senior Scientist and Distinguished Fellow Cell Biology Research Novus International
2001-2004	Senior Scientist and Senior Fellow Cell Biology Research Novus International
1996-2001	Director and Senior Fellow Cell Biology Research Novus International
1991-1995	Director and Fellow Cell Biology Research Novus International

1989-1991	Science Fellow Monsanto Company Animal Sciences Division Alimet Metabolism Group Drug Delivery Discovery Group
1981-1989	Research Specialist and Associate Fellow Monsanto Company Animal Sciences Division Alimet Metabolism Group Drug Delivery Discovery Group

PUBLICATIONS

Dibner, J.J. (1983) Utilization of supplemental methionine sources by primary cultures of chick hepatocytes. J. Nutr. 113:2116-2123.

Dibner, J.J. and A. Nakeff (1983) R3327 Prostate adenocarcinoma clonogenic cells: epithelial properties and hormone response. J. Natl. Cancer Inst. 70:1057-1066.

Dibner, J.J. and A. Nakeff (1983) Proliferative properties of the clonogenic cells of the R3327 prostatic carcinoma. In Vitro. 19:179-190.

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Dibner, J.J., R.A. Swick, R.R. Ontiveros, T.J. Ehmler and F.J. Ivey (1988) An update on recent research on the bioutilization of different sources of synthetic methionine activity. Monsanto Technical Symposium: Western Nutrition Conference Proceedings: pp. 7-12, September 13, 1988, Winnipeg.

Dibner, J.J., R.A. Swick, R.R. Ontiveros, T.J. Ehmler and F.J. Ivey (1988) Digestibility of Alimet and DL-Methionine. Monsanto Technical Symposia: Obregon and Guadalajara, Mexico, November 10-11, 1988 pp. 5-9.

Kitchell, M.L. and J.J. Dibner (1989) Rapid detection of proliferating cells using microwave fixation and a monoclonal antibody to bromodeoxyuridine. J. Histotechnology 12:101-103.

Dibner, J.J., R.C. Durley, J.G. Kostelc and F.J. Ivey. (1990) 2-Hydroxy-4-methylthio butanoic acid (HMB) is a naturally occurring methionine precursor in the chick. J. Nutr. 120:553-560.

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Dibner, J.J. and F.J. Ivey (1990) Hepatic protein and amino acid metabolism in poultry. Poult. Sci. 69:1188-1194.

Dibner, J.J. and F.J. Ivey (1990) Studies of the utilization and metabolism of 2-hydroxy-4-methylthio butanoic acid (HMB, Alimet) by the broiler chick. Monsanto Technical Symposia: Indonesia, Malaysia, Philippines, Taiwan and Thailand. September 1-15, 1989.

Dibner, J.J. and F.J. Ivey (1990) Utilization of 2-hydroxy-4-methylthio butanoic acid (MHA, Alimet) by the chicken. Monsanto Technical Symposium: Athens, Greece. April 19, 1989 pp. 39-48.

Knight, C.D., J.J. Dibner and F.J. Ivey (1991) Crystalline amino acid diets for chicks: History and future. Maryland Nutrition Conference Proceedings pp 19-28.

Dibner, J.J. and F.J. Ivey (1992). Capacity of chick liver enzymes relative to practical levels of supplemental methionine activity. Poult. Sci. 71:700-707.

Dibner, J.J., C.A. Atwell and F.J. Ivey (1992) Effect of heat stress on 2-hydroxy-4-(methylthio)butanoic acid (Alimet) and DL-methionine absorption measured *in vitro.* Poult. Sci. 71:1900-1910.

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